A MODEL OF SHORT-TERM SYNAPTIC FACILITATION RELYING ON BOTH FREE AND BOUND RESIDUAL CALCIUM. V. Matveev* and A. Sherman.
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Experiments have shown that short-term facilitation (STF) of synaptic response depends on the accumulation of Ca^{2+} in the presynaptic terminal. Ca^{2+} can accumulate either in a free form or bound to Ca^{2+} sensor(s) involved in vesicle release. We propose a new model for STF that depends on both free and bound residual Ca^{2+} (Regehr et al., 1994). In this model the putative Ca^{2+} sensor responsible for STF undergos a series of transformations upon Ca^{2+} entry, with a low-affinity Ca^{2+} binding step followed by a Ca^{2+} independent transition, which in turn is followed by a final high-affinity Ca^{2+} binding step. Due to the intermediate Ca^{2+} independent step, the final transition is still in progress after the microdomain of high $[Ca^{2+}]$ has dissipated. This makes STF sensitive to the low residual $[Ca^{2+}]$, in agreement with the evidence that exogenously applied buffers reduce PPF (Kamiya and Zucker, 1994), while the slow Ca^{2+} unbinding step ensures that the model predicts both F1 and F2 decay component of STF. The proposed mechanism also explains the observed super-linear growth of STF (Tang et al, 2000).

To implement the model we developed a program called CalC ("Calcium Calculator"), which will be made freely available. CalC solves differential equations describing Ca^{2+} entry through channels into a rectangular enclosure, and its diffusion, buffering and binding to Ca^{2+} sensors. The enclosure may contain rectangular obstacles representing vesicles or other diffusion barriers. An arbitrary number of fixed and mobile Ca^{2+} buffers may be included. CalC is driven by an ASCII definition file describing the simulation in simple, user-friendly format. CalC is written in C++ and currently runs on Linux and SGI platforms.